

What is claimed is:

1.

A stable, sterile, and injectable aqueous dispersion of a water-insoluble microdroplet matrix of mean diameter from about 50 nm to about 1000 nm consisting essentially of

- (a) between about 1% to about 15% of propofol;
- (b) between about 1% to about 8% of a propofol soluble diluent;
- (c) between about 0.5% to about 5% of a surface stabilizing amphiphilic agent;
- (d) of a pharmaceutically acceptable water-soluble polyhydroxy additive that acts as a tonicity modifier; and
- (e) provided the ratio of propofol to diluent is about 1:4 to about 1:0.1 and the ratio of propofol to amphiphilic agent is about 1:0.8 to about 1:2.5, and the composition has a viscosity of from about 0.8 to about 15 centipoise,

wherein the formulation

- prevents microbial growth, defined as no more than 0.5 log increase from the initial inoculum, of each of *Staphylococcus aureus* (ATCC 6538), *Escherichia coli* (ATCC 8739 and ATCC 8454), *Pseudomonas aeruginosa* (ATCC 9027), *Candida albicans* (ATCC 10231), and *Aspergillus niger* (ATCC 16403) for at least 7 days as measured by a test wherein a washed suspension of each said organism is added to a separate aliquot of a formulation at approximately 1000 colony forming units (cfu) per mL, at a temperature in the range 20-25°C, whereafter said aliquots are incubated at 20-25°C and are tested for viability of the microorganisms in the inoculated formulation as determined by counting the colonies of

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said organism after 24, 48 hours and 7 days or other time;

■ results in little or no irritation at the site of injection wherein said composition is administered as a single dose of 12.5 mg/kg, given on the basis of body weight, 1-3 days over a period of approximately 30 seconds, in such that no visual increase in the diameter of the nodule is observed 48hrs post injection.

The composition of claim 1 wherein the surface stabilizing agent is one or more natural or synthetic surface modifiers selected from the group consisting of non-ionic surfactants, cationic surfactants, ionizable phospholipids or cholesterol or a mixture of these agents, the total quantity of the amphiphilic agents being such that the total amphiphilic agent is about 1:0.8 to about 1:2.5 and the type of individual amphiphilic agents are selected to provide that:

- the composition has a non-existent or minimum potential for irritation to human or animal blood, and
- the irritation to the tissues at the site of injection is minimized, and
- the composition elicits an anesthetic effect in warm-blooded human subjects upon intravenous administration.

The composition of claim 1 wherein the propofol-soluble agent is a natural fatty acid, triglyceride thereof or other suitable ester.

The composition of claim 1 wherein the ratio of propofol to propofol-soluble diluent is from about 1:3 to about 1:0.5.

- said organism after 24, 48 hours and 7 days or other time;
- results in little or no irritation at the site of injection wherein said composition is administered as a single dose of 12.5 mg/kg, given on the basis of body weight, 1-3 days over a period of approximately 30 seconds, in such that no visual increase in the diameter of the nodule is observed 48hrs post injection.
- The composition of claim 1 wherein the surface stabilizing agent is one or more natural or synthetic surface modifiers selected from the group consisting of phospholipids, cholesterol, or a mixture of these, wherein the total quantity of the amphiphilic agents being such that the ratio of the amphiphilic agent is about 1:0.8 to about 1:2.5 and the type of individual amphiphilic agents are selected to provide that:
- (i) the composition has a non-existent or minimum potential for irritation to human or animal blood, and
 - (ii) the irritation to the tissues at the site of injection is minimized, and
 - (iii) the composition elicits an anesthetic effect in warm-blooded human subjects upon intravenous administration.
- The composition of claim 1 wherein the propofol-soluble agent is a natural fatty acid, triglyceride thereof or other suitable ester.
- The composition of claim 1 wherein the ratio of propofol to propofol-soluble diluent is from about 1:3 to about 1:0.5.

- said organism after 24, 48 hours and 7 days or other time;
- results in little or no irritation at the site of injection wherein said composition is administered as a single dose of 12.5 mg/kg, given on the basis of body weight, 1-3 days over a period of approximately 30 seconds, in such that no visual increase in the diameter of the nodule is observed 48hrs post injection.
- The composition of claim 1 wherein the surface stabilizing agent is one or more natural or synthetic surface modifiers selected from the group consisting of phospholipids, cholesterol, or a mixture of these, wherein the total quantity of the amphiphilic agents being such that the ratio of the amphiphilic agent is about 1:0.8 to about 1:2.5 and the type of individual amphiphilic agents are selected to provide that:
- (i) the composition has a non-existent or minimum potential for irritation to human or animal blood, and
 - (ii) the irritation to the tissues at the site of injection is minimized, and
 - (iii) the composition elicits an anesthetic effect in warm-blooded human subjects upon intravenous administration.
- The composition of claim 1 wherein the propofol-soluble agent is a natural fatty acid, triglyceride thereof or other suitable ester.
- The composition of claim 1 wherein the ratio of propofol to propofol-soluble diluent is from about 1:3 to about 1:0.5.

5. The composition of claim 1 wherein the ratio of propofol to the amount of propofol-soluble diluent is from about 1:2 to about 1:1.
6. The composition of claim 1 wherein the propofol-soluble diluent is a mixture of medium-chain triglyceride and vegetable oil.
7. The composition of claim 6 wherein the ratio of medium-chain triglyceride to vegetable oil is from 1:3 to 3:1.
8. The composition of claim 1 wherein the water-insoluble matrix consists of a mixture of the amphiphilic agents of claim 3 and propofol-soluble diluents of claims 4-7 and propofol.
9. The composition of claim 1 wherein the composition contains about 2% to about 10% of propofol.
10. The composition of claim 1 wherein the composition contains a pharmaceutically acceptable water-soluble polyhydroxy additive that provides the propofol containing dispersion with an osmolality of about 250 to about 700 milliosmolal.
11. The composition of claim 1 wherein the osmolality is about 300 to about 500 milliosmolal.
12. The composition of claim 1 wherein the viscosity is from about 2 to about 5 centipoise.

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13. The method of reducing or substantially completely eliminating irritation upon injection of formulations containing propofol by administering a stable, sterile, and antimicrobial, aqueous dispersion of water-insoluble microdroplet matrix of mean diameter from about 50 nm to about 1000 nm consisting essentially of about 1% to about 15% of propofol as the active ingredient, up to about 7% of a propofol soluble diluent, and about 0.8% to about 4% of a surface stabilizing amphiphilic agent, and the aqueous phase of the composition consisting of a pharmaceutically acceptable water-soluble polyhydroxy tonicity modifier, the composition being devoid of additional bactericidal or bacteriostatic preservative agents, provided the ratio of propofol to diluent is about 1:4 to about 1:0.1 and the ratio of propofol to amphiphilic agent is about 1:0.8 to about 1:2.5, and the composition has a viscosity of from about 0.8 to about 15 centipoise.
14. The method of inducing anesthesia comprising administering to a subject in need of same an anesthetic inducing amount of a stable, sterile, and antimicrobial injectable aqueous dispersion of a water-insoluble microdroplet matrix of mean diameter from about 50 nm to about 1000 nm consisting essentially of about 1% to about 15% of propofol as the active ingredient, up to about 7% of a propofol soluble diluent, and about 0.8% to about 4% of a surface stabilizing amphiphilic agent, and the aqueous phase of the composition consisting of a pharmaceutically acceptable water-soluble polyhydroxy tonicity modifier, the composition being devoid of additional bactericidal or bacteriostatic preservative agents, provided the ratio of propofol to diluent is about 1:4 to about 1:0.1 and the ratio of propofol to amphiphilic agent is about 1:0.8 to about 1:2.5, and the composition has a viscosity of from about 0.8 to about 15 centipoise.

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